





# **PCT**

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

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ans	INTERNATIO	NAL PRELIMINA	RY EXAMIN	ATION REPORT
		(PCT Article 36	and Rule 70)	
Applicant's or agent's fi	<b>!</b>	FOR FURTHER ACTION	ON See Notifi Preliminary	ication of Transmittal of Internation Examination Report (Form PCT/IPEA/41
International application PCT/CH2003		nternational filing date (date 13 October 2003 (		Priority date (day/month/year) 14 October 2002 (14.10.2002)
International Patent Clas C07K 14/54	ssification (IPC) or nati	onal classification and IP	C	
Applicant		F. HOFFMANN-LA	ROCHE AG	
2. This REPORT  This rep amende 70.16 an	port is also accompanied and are the basis for the A and Section 607 of the A	8 sheets, inc	ets of the descript ontaining rectific under the PCT).	tion, claims and/or drawings which have b cations made before this Authority (see F
3. This report con  I	Basis of the report Priority Non-establishment of Lack of unity of invertications and explana Certain documents of Certain defects in the	ntion under Article 35(2) with r tions supporting such stat	egard to novelty, ement	step and industrial applicability inventive step or industrial applicability;
Date of submission of	f the demand May 2004 (11.05.2		Pate of completion	n of this report November 2004 (04.11.2004)
Name and mailing ad	dress of the IPEA/EP	.4	authorized office	r
Facsimile No.		1,	Celephone No.	

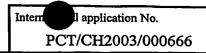


#### INTERNATIONAL PRELIMINARY EXAMINATION REPORT

## PCT/CH2003/000666

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pages	1-43	, as originally filed
pages _		, filed with the demand
pages _	, filed with the letter of	
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pages _	1-38	, as originally filed
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the draw	rings:	
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internation see elemen the lan the lan the lan or 55.3	al application was filed, unless otherwise indicated under this item.  Is were available or furnished to this Authority in the following language  guage of a translation furnished for the purposes of international search (under Rule guage of publication of the international application (under Rule 48.3(b)).  guage of the translation furnished for the purposes of international preliminary e ).	which is: 23.1(b)).  xamination (under Rule 55.2 and/
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This rebeyond this report of 70.17).	the claims, Nos the drawings, sheets/fig  eport has been established as if (some of) the amendments had not been made, sin if the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**  sheets which have been furnished to the receiving Office in response to an invitation of the control	tion under Article 14 are referred to t contain amendments (Rule 70.16
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III. Non-	establishment of opinion with regard to novelty, inventive step and industrial applicability
1. The condust	questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be rially applicable have not been examined in respect of:
	the entire international application.
$\boxtimes$	claims Nos
becau	se:
$\boxtimes$	the said international application, or the said claims Nos. 27, 28 relate to the following subject matter which does not require an international preliminary examination (specify):
	the description, claims or drawings (indicate particular elements below) or said claims Nos.
	are so unclear that no meaningful opinion could be formed (specify):
	the claims, or said claims Nos are so inadequately supported by the description that no meaningful opinion could be formed.
$\boxtimes$	no international search report has been established for said claims Nos
2. A me seque	aningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid ance listing to comply with the standard provided for in Annex C of the Administrative Instructions:
	the written form has not been furnished or does not comply with the standard.
	the computer readable form has not been furnished or does not comply with the standard.

#### INTERNATIONAL PRELIMATION REPORT

Supplemental Box

(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: Box III.1.

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The applicant is advised that claims or parts of claims relating to inventions in respect of which no international search report (ISR) has been established cannot normally be the subject of an international preliminary examination (PCT Rule 66.1(e)). In its capacity as International Preliminary Examining Authority the EPO generally will not carry out a preliminary examination for subjects that have not been searched.

As already mentioned in the ISR, the search in relation to the current claims 1 to 38 was directed to the parts of the claims that appear to be clear, supported or disclosed, that is the parts concerning the fusion proteins that contain an IL-15 with the amino acid sequence defined in SEQ ID NO:1.

Since the International Examining Authority shares the opinion of the International Searching Authority, the international preliminary examination was restricted to this searched subject matter defined above.

Claims 27 and 28 relate to subject matter which, in the opinion of this Authority, falls under PCT Rule 67.1(iv). Consequently, no expert opinion has been established in respect of the industrial

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Supplemental B To be used when	Box en the space in any of the preceding boxes is not sufficient)	
	Box III.1.	
	applicability of the subject matter of said claims	
	(PCT Article 34(4)(a)(i)).	
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#### INTERNATIONAL PRELIMINARY EXAMINATION REPORT

Internation polication No.
PCT/CH 03/00666

Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement					
1. Statement					
Novelty (N)	Claims	1-38 (as far as examined)	YES		
• • •	Claims		NO		
Inventive step (IS)	Claims	1-38 (as far as examined)	YES		
2.0	Claims		_ NO		
Industrial applicability (IA)	Claims	1-26, 29-38	_ YES		
	Claims		NO		

- 2. Citations and explanations
  - Reference is made to the following documents:
    - D1: PETTIT DEAN K ET AL: JOURNAL OF BIOLOGICAL CHEMISTRY, Vol. 272, No. 4, 1997, pages 2312-2318
    - D2: ZHENG X X ET AL: JOURNAL OF IMMUNOLOGY, 163, No. 7, 1 October 1999 (1999-10-01), pages 4041-4048
    - D3: RUECKERT R ET AL: EUROPEAN JOURNAL OF

      IMMUNOLOGY, WEINHEIM, DE, Vol. 28, No. 10,

      October 1998 (1998-10), pages 3312-3320
    - D4: WO 97/41232 A (BETH ISRAEL HOSPITAL) 6 November 1997
  - 2. Clarity and support from the description (PCT Articles 5 and 6):

The current claims 1 to 38 relate to a fusion protein that is characterised only by a desirable characteristic or property, namely that it contains a wild-type IL-15, since the amino acid sequence of the wild-type IL-15 is not defined. The claims are therefore unclear, since the amino acid sequence is an essential feature of the invention.

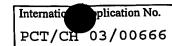
2.2 As already mentioned in the application, it is totally surprising that a fusion protein consisting of a wild-type IL-15 and an Fc fragment has an antagonistic effect. Thus, for example, the results in example 5 contradict the results shown by Zheng et al. (document D2) and Rueckert et al. (document D3, which discloses the subject matter of the disclaimer).

When an invention is based on a surprising effect, the features that produce that effect must be part of the claimed subject matter. Since the application discloses only one fusion protein with this property (namely wild-type IL-15-mlgG2a with the amino acid sequence defined by SEQ ID NO:5) and does not indicate why this fusion protein has this effect and similar, known fusion proteins do not, it is not clear to a person skilled in the art what other fusion proteins could have this effect.

Consequently, there is no basis for generalising this example and the subject matter of **claim 1** is supported only insofar as it relates to a fusion protein with the amino acid sequence defined by SEQ ID NO:5 and should be restricted accordingly.

- 2.3 The applicant should note that the European examining procedure does not allow disclaimers for embodiments which do not solve the problem of interest ("non-working embodiments"; see G0001/03, reasons for decision, paragraph 2.5).
- 2.4 Claims 23 to 25, which are directed to a second medical indication, are inadmissible under PCT Article 6. The therapeutic application is defined

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in functional terms by an active mechanism ("IL-15-mediated events") which does not allow any practical application in the form of a defined actual treatment of a pathological illness (disease).

In addition, in respect of these claims, as well as claim 26, the use of human or animal tissue or of a human or animal organ is not supported by the description (PCT Article 5).

2.5 Claim 30 does not meet the requirements of PCT
Article 6 because the subject matter for which
protection is sought is not clearly defined. The
claim attempts to define the subject matter in terms
of the result to be achieved (i.e. steps b) and c)),
but in so doing merely states the problem to be
solved, without specifying the technical features
needed to achieve this result.

In addition, step 4 is not restricted to in vitro treatment and therefore the claim also covers an in vivo treatment method.

2.6 The PCT Contracting States do not have uniform criteria for assessing the industrial applicability of claims 27 and 28 in their present form.

Patentability may also depend on the wording of the claims. The EPO, for example, does not recognise the industrial applicability of claims to the medical use of a compound; it may, however, allow claims to the first medical application of a known compound or to the use of such a compound in the manufacture of a drug for a new medical application.

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- 3. Novelty and inventive step (PCT Article 33(2) and (3))
- 3.1 Insofar as it has been examined, the subject matter of main claim 1 is novel.
- 3.2 Since the prior art does not indicate that a wildtype-IL-15-mlgG2a fusion protein would have an
  antagonistic effect, the subject matter of main
  claim 1, insofar as it is restricted to this fusion
  protein, is inventive.
- 4. Additional observations:
- 4.1 Claims 17, 18 and 32 cover embryonic stem cells and claim 21 covers parts of the human body. In the opinion of this IPEA, these claims are contrary to public order and morality and are therefore not acceptable.